SCIENCE

VOL. 100 FRIDAY, JULY 21, 1944 No. 2586

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SCIENCE: A Weekly Journal devoted to the Advancement of Science. Editorial communications should be sent to the editors of SCIENCE, Lancaster, Pa. Published every Friday by

THE SCIENCE PRESS

Lancaster, Pennsylvania

Annual Subscription, $6.00 Single Copies, 15 Cts.

SCIENCE is the official organ of the American Association for the Advancement of Science. Information regarding membership in the Association may be secured from the office of the permanent secretary in the Smithsonian Institution Building, Washington 25, D. C.

PREVENTIVE MEDICINE: AN ATTEMPT AT A DEFINITION[1]

By GEDDES SMITH and LESTER J. EVANS, M.D.

THE COMMONWEALTH FUND

THE relief of pain is an important function of medicine. It is often the physician's first duty to "make the patient comfortable." As soon as clinical medicine gets beyond this palliative stage, however, it becomes preventive medicine. The major function of the physician is to hold disease in check lest disability or death result from it; in other words, to prevent the graver consequences of dysfunction. While it is possible to distinguish between preventive and palliative medicine, it is difficult and generally unprofitable to draw a line between preventive and curative medicine. To cure disease is to cut it short—to prevent its continuance—and so to prevent the consequences of its continuance. Preventive medicine might logically be defined as *all* medicine that seeks to alter the course of disease or to better the patient's physiological status.

[1] A memorandum prepared in connection with the activities of The Commonwealth Fund.

For practical purposes, however, the term has commonly been restricted to mean the intervention of the physician or his technical allies in a limited range of situations in which specific diseases can be warded off or specific deterioration of the patient's condition can be forestalled. Such service is possible (at the present stage of medical science) at three different levels which will be considered in turn.

The most conspicuous field for the operation of preventive medicine is communicable disease. All disease is the result of a chain of causes, but in infectious diseases a uniformly essential link in this chain is found outside the body and, in varying degree, is accessible to attack. The external cause can be neutralized by destroying the infective agent outside the body (*e.g.*, killing typhoid bacilli in water) or by specifically increasing the body's resistance to a particular invader (as by immunization against diphtheria). If more were known about the internal fac-

tors in the causation of communicable disease—the factors which make one patient susceptible while another remains resistant—preventive medicine could no doubt do a better job in this field, but the rewards of diligent attack on the accessible external factors are very great (*e.g.*, the establishment of virtual control over yellow fever).

Preventive medicine occupies a like position with respect to the diseases caused by dietary and particularly vitamin deficiencies. Clear-cut prevention of a specific disease is sometimes possible (*e.g.*, the prevention of scurvy by including lime-juice in British naval rations, begun in 1795) and the wide extension of preventive measures of a similar sort waits only upon the growth of exact nutritional information and the development of adequate tests for marginal deficiencies.

The first level of preventive medicine is then the prevention of obviously preventable diseases. But if preventive medicine be limited to this function much of its significance is lost. It has an important role to play in curable chronic diseases whether or not these are preventable. This is true with respect to the two great chronic disabling diseases in the communicable group—syphilis and tuberculosis. Quite apart from the need for averting the incidence of these infections by public health measures (which of course form part of preventive medicine), preventive medicine is concerned with their early recognition and treatment lest they go on to disable or kill the patient. Prompt and aggressive treatment—a purely curative process—takes on a strongly preventive coloring because it may forestall serious deterioration or death. This is true also of cancer, a non-preventable disease of unknown cause which can nevertheless be cured in many instances by surgical removal or radiological destruction of the lesion. The full use of modern diagnostic facilities permits such intervention at a profitable stage in many cases of cancer which would otherwise go unrecognized until they were incurable. The gastro-intestinal x-ray study which a careful diagnostician orders when confronted with certain abdominal symptoms is thus an important tool of preventive medicine. There are indications, too, that some psychoses will yield to treatment with convulsants (insulin, electricity, etc.) if such treatment is given early enough, and preventive medicine may yet concern itself effectively with frank mental disease as well as with mental hygiene (of which more later). It is the time-factor which makes these conditions of special interest to preventive medicine; early and successful intervention pays large dividends in the prevention of later morbidity and mortality. At this second level, however, preventive medicine is handicapped by the paucity of methods suitable for routine use in the prompt recognition of incipient chronic disease, and so must be largely opportunistic.

It is possible to prevent the preventable diseases, and to prevent some of the consequences of curable chronic diseases. It is also possible to prevent or delay some of the consequences of non-preventable and non-curable diseases, and this is a third level of preventive medicine. Cardiovascular disease is certainly not preventable in the sense that malaria is preventable, and it is not curable in the sense that cancer is sometimes curable. So far as is now known, there is no extrinsic factor accessible to attack, no ruling deficiency in diet, no localized lesion which can be extirpated. It lies enmeshed in a web of physiological controls which as yet the investigator can not trace. And yet because it is a chronic condition intimately affecting the daily behavior of the patient preventive medicine has a notable opportunity to influence its course. The task is to fit the patient's way of life to his physical resources so that he will live as usefully, as happily, and as long as his condition permits and will not squander his resources in overexertion or underexertion or in emotional conflict. Telling a man with an overstrained heart to stop lugging ashcans up and down cellar stairs is preventive medicine of a very simple sort. Releasing him from tensions growing out of family incompatibility or the fear of early death is a subtler way of accomplishing a like end. Both procedures tend to prevent the waste of human energy, if not the exacerbation of the disease itself.

This fairly specific task merges into a more general one. Since the hazards of communicable disease (partly because of better control of the environment, partly because of the successes of chemotherapy) are definitely on the wane, the major task of preventive medicine now is the maintenance of physiological tone in the hope of delaying, mitigating, or if possible preventing those degenerative and senescent changes which account for most deaths in the later adult years. Physiological tone is so intimately connected with emotional balance that psychiatry of a dynamic sort—the sort that addresses itself to the relief of emotional stresses in non-psychotic persons—is an indispensable ally of preventive medicine at this level. Yet it can not be said that in general the natural history or the basic causes of these degenerative changes are well enough known to give the clinician a clear course to steer by. He must feel his way. For the present preventive medicine must stay close to the early-recognition-prompt-intervention-protective-regime range of clinical service, and clear-cut prevention of specific disease processes or their ultimate consequences is seldom possible. However, medicine is an art that has always pushed beyond the frontiers of medical

science and this range of service is well worth cultivation even if it remains empirical and falls short of complete success.

As one multiplies the possible applications of preventive care to the treatment of incipient or established disease, preventive medicine becomes all but indistinguishable from good clinical medicine in general. Better diagnosis, prompt intervention in diseases or disorders which can be arrested or relieved, the intelligent adjustment of the patient's behavior to his physical and psychological assets—these are the objectives of good practice everywhere and under any name. The logical culmination of what is called preventive medicine, however, transcends the traditional function of medicine, which is to heal the sick. Hygiene is a slightly tarnished word, perhaps because it has been bandied about by relatively unskilled and sentimental people before its scientific underpinnings have become quite secure. But the building and maintenance of health—that is, optimum physiological status—is a goal not unworthy of medical art and science. When genetics, physiology and psychology can be integrated and put to work to develop top-flight human beings and keep them at their best throughout a normal life-span, the prevention and cure of disease will fall into their proper place as subsidiary and not primary objectives, and medicine will become constructive rather than remedial or preventive. All this at the moment has a utopian sound, and a vast amount of investigation is needed before it can become a reality. The best indication that it might become a reality is the progress pediatrics has already made toward focussing scientific and clinical attention on normal growth and development.

Some degree of professional reorientation is needed even at present levels of preventive medicine. It is impossible for a physician to grasp the opportunities already mentioned in these notes without taking rather more initiative than physicians have usually felt free to take with their patients, and without thinking in terms of persons who are patients rather than in terms of diseases which occur in patients. The last generation in medicine thought hard about diseases and learned much about them, and worked hard at the physiology of organs and tissues. The era of scientific medicine has been devoted to the intensive exploration of narrowly defined areas. This was inevitable; exact knowledge could have been gotten in no other way. Unfortunately this singleness of purpose has created as a by-product a sharp parochialism in medicine and in medical schools, so that above the general practitioner level (or below it) there is growing lack of cohesion and integration. Medicine is too much departmentalized. In dealing with communicable diseases preventive medicine seeks to reconcile the clinical attitude toward the feverish child with the public health attitude toward a disease that sweeps through the crowd. In dealing with chronic and especially degenerative diseases it seeks to integrate the probing of physiological details with an overall awareness of the patient's life as a problem in itself. The practice of preventive medicine requires a change in viewpoint quite as much as the acquisition of specific techniques.

The teaching of preventive medicine is therefore a complex task. The techniques involved would not by themselves justify the establishment of a separate department to teach them. The purpose of such a department is to influence the flavor and emphases of medicine rather than to alter its content. Once established, however, it attracts to itself various tasks, some central to its purpose, some assigned to it merely for convenience.

The control of communicable disease has an obvious place in this curriculum. Since that involves organized public health service, the department of preventive medicine needs contact with public health agencies and is responsible for acquainting the medical student with their work at large and with public health procedures which form part of private practice—notably the techniques of immunization. The part which the individual physician has to play in controlling an epidemic may be small, but a knowledge of the way in which communicable disease spreads is or should be a stimulus to better clinical management of such disease in the individual patient. For this reason, and for the contribution which the study of disease as a mass phenomenon can make to medical philosophy, the study of epidemiology is usually included in the preventive medicine curriculum. Biostatistics finds place there too, partly because it is an essential tool of epidemiology, partly because it is useful to any physician who expects to do scientific investigation or to evaluate the scientific work of other clinicians. It is taught in the department of preventive medicine chiefly because no other department has recognized its importance or has been competent to teach it.

More closely related to the major objectives of preventive medicine is the task of personalizing clinical medicine. This the department would have to undertake for its own ends even if the job had not gone by default in other departments where it is equally needed. Poverty and social maladjustment are certainly not preventable in terms of any individual doctor's efforts, but the effects of these factors and of emotional stresses generally on the physical status of the patient greatly need to be brought to the attention of the medical student. Hence the courses, now

familiar in a number of schools, in which senior medical students visit the homes of clinic patients to study and report on their environment and the emotional background of their diseases. These are five-finger exercises in personalized clinical care; they should be reinforced by more difficult and more significant tasks set by the student's instructors in psychiatry.

The core of preventive medicine—the adjustment of the individual patient to his physiological equipment and status—can hardly be taught successfully in didactic courses. The student needs to see his instructor handling patients in the clinic and at the bedside in a way that makes full use of the resources of medicine for bringing about such an adjustment—resources which are still all too meager for the infinite variety of the task. The department of preventive medicine can not hold itself aloof from other clinical departments if it is to do and to promote such teaching: its members must take their places on the clinical team of the teaching hospital and do their part to enrich general medicine rather than attempting to build up a separate discipline.

The task of the department of preventive medicine, in sum, is then:

(1) To teach the medical student what he needs to know about available techniques for the prevention of communicable disease;

(2) To give him an understanding of epidemiology and quantitative methods in medical science;

(3) To sensitize him to opportunities for arresting the development of non-communicable disease;

(4) To make him aware of the patient as a person and thus to initiate him more fully into the art of medicine; and ultimately

(5) To show him how medicine can help to maintain or increase productive energy in both normal and handicapped individuals.

It will be seen that these objectives can be translated only in part into a formal curriculum. The more significant service of the professor of preventive medicine is to act as catalyst—offering new points of view, broadening clinical concepts, stretching the imagination, and nourishing the philosophy of both his students and his colleagues.

OBITUARY

WILLIAM SPENCER CARTER

1869–1944

INCREASINGLY significant is the influence of American medicine in the development of medical training and research in outlying parts of the world. A notable pioneer in transfusing the best of American medical idealism and methodology in the Pacific area was William Spencer Carter, who died in Auburndale, Mass., on May 12, 1944.

Dr. Carter was a leader in the development of clinical physiology, an outstanding medical administrator, and a generous guide in promoting medical education and research.

Born in Warren County, N. J., on April 11, 1869, Dr. Carter graduated in medicine from the University of Pennsylvania in 1890. As a medical student he had worked in the private laboratory of Dr. Isaac Ott at Easton, Pa., on cerebral heat centers. Following the receipt of his degree in medicine he became demonstrator of pathology at the University of Pennsylvania. In 1894 he was assistant professor of physiology at Pennsylvania, and in 1897 he came to Galveston as professor of physiology at the University of Texas Medical Branch. At Galveston Dr. Carter organized one of the first physiology laboratories in the South.

Dr. Carter's executive ability was recognized in 1903 when he succeeded the late Dr. Allen J. Smith as dean of the University of Texas School of Medicine, Dr. Smith having returned to the University of Pennsylvania. Under Dr. Carter's administration the University of Texas School of Medicine developed effective leadership in medical education and research in the Southwest in intimate association with the John Sealy Hospital.

At the request of the Rockefeller Foundation, the University of Texas lent Dr. Carter in 1922 to the University of the Philippines, Manila, where he assisted in the organization and development of the medical school. In 1923 Dr. Carter became associate director of the Medical Sciences Division of the Rockefeller Foundation. As such, he made an important survey of medical education in the Philippines, Australia, South Africa, Java and New Zealand. In 1925 Dr. Carter became acting director of Peking Union Medical College, where he assisted in the notable expansion of medical educational efforts in China. In 1926 he went to India to make an official survey with recommendations for the future of medical education in that area. He was instrumental in the establishment of the School of Tropical Medicine at Calcutta.

Dr. Carter retired from work with the Rockefeller Foundation in 1934. Shortly thereafter he returned to the University of Texas to serve again as dean of the Medical Branch until 1938, when he retired to his home in Massachusetts.

Dr. Carter had come originally to Galveston in connection with yellow fever work. At the University

of Texas Medical Branch he inaugurated courses in hygiene and public health, and founded the department of pharmacology. He succeeded in adding a number of buildings to the plant of the John Sealy Hospital and assisted in promoting the building of the special out-patient clinic and Children's Hospital.

In 1892 Dr. Carter won the Boylston Prize for his investigations on leucocytosis and blood serum. In 1903 he was awarded the Alvarenga Prize. While his publications were not many, they were important and stimulating. His study of the physiological action of the poisons from various species of *amanita* in 1901 remains a classic. He was among the first to study the pronounced general physiological disturbance resulting from ether anesthesia. His studies on intraspinal pressure were important in practical application in withdrawing cerebrospinal fluid and in making intraspinal injections. During World War I he made important investigations on the use of citrated blood for transfusion. His studies on the function of renal epithelium stimulated much subsequent work.

In the field of public health Dr. Carter was a pioneer in promoting measures for the control of tuberculosis. He advocated the registration of all cases, the control of milk supply through pasteurization, the establishment of special hospitals and a broad educational campaign designed to acquaint the people with the dangers of tuberculosis, the way it spreads and the methods of preventing it. He was among the first to emphasize the dangerous sequelae of mild, acute infections such as scarlet fever.

Dr. Carter was a member of the National Board of Medical Examiners, the American Physiological Society and the College of Physicians of Philadelphia. He was prominent in the affairs of the American Medical Association, and a respected public leader in promoting a reasonable appreciation of the practical significance of medical affairs. Dr. Carter made lasting friendships wherever he went, and inspired all who knew him to strive more effectively for healthy human welfare.

A stimulating medical teacher and executive, Dr. Carter greatly influenced the course of medical education and medical effort over a wide area of the world. He was the type of medical leader of which many indeed are needed these days.

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LOSSES IN PERSONNEL OF SOVIET BOTANY DURING THE WAR

THE last mail coming from the U.S.S.R. after a very long intermission brought sad news of heavy losses in the ranks of Soviet botanists during three years of the war. Some of them are direct results of military action and some apparently may be attributed to severe sufferings caused by the war, especially in besieged Leningrad and its vicinity, and to natural causes.

The following notes give some biographical data on the most important of deceased botanists.

The truly irreparable loss for botanical science is the death of Evgenii Vladimirovich Wulff (1885–1941), one of the most outstanding and erudite of Russian botanists, killed by a bomb fragment on December 21, 1941, in Leningrad. Wulff, who at the time of his death was senior specialist and curator of the Herbarium of Cultivated Plants, Geographical Department, Institute of Plant Industry, was active in many branches of botanical science: historical plant geography, flora and vegetation of Crimea, taxonomy of cultivated plants and history of botany. His more important publications include: "Introduction to Historical Plant Geography" (Russian, 1932, 1933 and English translation 1943); "Historical Plant Geography" (Russian, 1936) and "Flora taurica," 3 fasc. (1927–30). A more extensive biographical sketch of Wulff will appear soon in *Chronica Botanica*.

Dr. Vladimir Petrovich Maleev (1894–1941), who died on December 21, 1941, was one of the best authorities on the flora and vegetation of the Caucasus and Crimea and the acclimatization of subtropical plants. He was born on February 24, 1894, at Kharkov and educated in the same city, graduating in 1917. After teaching biology and botany for some years, he served in various botanical institutions in the Caucasus, 1923–26, in Nikita Botanical Garden in Crimea, 1926–30, and in 1931 joined the Institute of Plant Industry in Leningrad. In 1934 he became senior botanist of the Geobotanical Department of the Institute of Botany. He made several exploring trips to the Caucasus, 1919–26, 1934–35, 1936–38 and 1941, and to Tien Shan in 1939. He is the author of more than 60 botanical works, including "Vegetation of the Black Sea Region" (Russian, 1940); "Tertiary relicts of the flora of western Caucasus" (Russian, 1941), etc.

Dr. Vadim Sergeevich Poretsky (1893–1942), professor of plant morphology and systematics at Leningrad University, died on February 8, 1942, in Vaibokala. His greatest contribution to science is his work on the taxonomy of cryptogams and the study of fossil diatoms of Leningrad Province and Ladoga Lake. He was born at Vazo, Esthland, and graduated from St. Petersburg University in 1917. He became assistant in botany at Perm University in the same year, and in 1921 removed to Leningrad, where he was assistant professor of botany of the Institute of Agriculture and since 1923 was connected with the Leningrad Botanical Garden and University.

Dr. Afanasii Nikolaevich Danilov (1879–1942), senior specialist of the ecological department of the Institute of Botany, who died in January of 1942 in Leningrad, was an old plant physiologist well known for his works on symbiosis of lichens and phytosynthesis of cryptogams and higher plants. He was born in Mogilev and graduated in 1911 from St. Petersburg University. In the same year he became conservator of the Tifliss Botanical Garden but in 1914 returned to St. Petersburg as a member of the staff of the Botanical Garden. In the Institute of Botany he worked first in the cryptogamic department and since 1937 in the department of ecology. His writings include: "La symbiose, comme facteur de l'évolution" (1921); "Hydrochrome der Cyanophyceen und Florideen" (1922) and many other articles in periodicals.

Dr. Ivan Ivanovich Sprygin (1873–1942), well-known geobotanist, was born on July 5, 1873, at Penza and died on October 1, 1942, in the same city. After his graduation from Kazan University he taught natural history from 1897 to 1919 and made several exploring trips to Penza and Saratov provinces and to Turkestan. He was professor of botany of the Middle Asia University (Tashkent), 1920–21, and director of the Penza sanctuary, 1925–38, and the Botanical Museum, 1938–40. He is the author of many articles on plant geography.

Konstantin Illarionovich Solonevich (1903–42), geobotanist and specialist on the flora of arctic and northern regions, was born on March 12, 1903, at Tosno and educated at Leningrad, attending first the Institute of Agriculture and then the university, from which he was graduated in 1930. He explored Kola Peninsula in 1927, 1932–34 and 1935–36, Karelia in 1928–29 and directed paleobotanical investigation of the Leningrad region in 1935–36. He was connected with the geobotanical department of the Institute of Botany until his death on February 9, 1942, in Borisova Griva. His publications include "Ein Beitrag zur Vegetation des nordöstlichen Teils des Lowosero Gebirges" (*Kola-Halbinsel*) (1936); "Notes sur la régression de l'aire du pin en la péninsule de Kola" (1940), etc.

Nikolai Fedorovich Komarov (1901–42), geobotanist and student of steppe vegetation, was born in 1901 at Tver and, after teaching for some years in lower schools, entered the University of Voronezh and was graduated in 1926. He served in the Museum of Natural History of Voronezh and lectured on botany and soil science in the Institute of Agriculture and the university of the same city, becoming docent of botany in 1932. Since 1935 he was associated with the Institute of Botany, working first in the Botanical Museum and then in the department of raw materials. He is the author of "Nature of Voronezh Province" (Russian, 1929); "Les unités géobotaniques de Voronège et de Koursk" (1940); "Relief and Geographical Distribution of Plants" (Russian, 1940) and some other articles.

In the death of Woldemar H. (Vladimir Andreevich) Tranzschel (1868–1942) plant science lost one of the most prominent mycologists of our time. We have to add only a few facts to the appreciation of his work which has already been published in SCIENCE (99: 443, 1944) by Rolf Singer. He was born on January 16, 1868, at St. Petersburg and educated in the same city. After his graduation in 1889, he served as assistant in botany and curator of the Botanical Museum of the St. Petersburg University, 1891–92, assistant in botany at the Institute of Forestry, 1892–98, and assistant in plant morphology and systematics at Warsaw Universiy, 1898–99. In 1900 he returned to St. Petersburg as curator of the Botanical Museum of the Academy of Sciences and since that time was connected with this institution until his death late in 1942. He founded the cryptogamic herbarium which, under his guidance, became one of the best in Europe. But he was not only a herbarium scientist, he collected extensively in Viborg (Vipuri), Novgorod and St. Petersburg provinces, in Turkestan, the Far East and the Crimea. He was deservedly considered a great authority on Uredinales and the results of his 50 years' study are incorporated in his masterpiece, "Rusts of the U.S.S.R." (Russian, 1938).

VLADIMIR C. ASMOUS

ARNOLD ARBORETUM,
HARVARD UNIVERSITY

RECENT DEATHS

DR. JOSEPH BRENNEMANN, until a year ago professor of pediatrics and head of the department of the School of Medicine of the University of Southern California, died on July 2. He was in his seventy-second year.

WILLIAM CATESBY JONES, of the division of chemistry of the State Department of Agriculture of Virginia, died on July 10 at the age of sixty-three years.

ALEX. W. MCCOY, consulting geologist of Tulsa, Okla., died on July 1 at the age of fifty-five years.

DR. A. H. REGINALD BULLER, emeritus professor of botany and founder of the department of botany of the University of Manitoba, died on July 3. He was in his seventieth year.

J. R. NORMAN, deputy keeper in the Department of Zoology of the British Museum (Natural History), died on May 26 at the age of forty-five years. Since early in the war he had been in charge of the Tring Museum, now a branch of the British Museum.

THE death is announced of Professor J. Shaw Dunn, who has held the chair of pathology in the University

of Glasgow since 1936, in succession to Sir Robert Muir.

AN Associated Press dispatch reports that William Lutley Sclater, zoologist and ornithologist, formerly director of the South African Museum at Cape Town, has been killed by a German flying bomb. He was eighty-one years old.

SCIENTIFIC EVENTS

RECENT CONTRIBUTIONS OF THE PREVENTIVE MEDICINE SERVICE OF THE U. S. ARMY

THE objectives of the Preventive Medicine Service of the Office of the Surgeon General are the maintenance and conservation of the health of the Army through the prevention and control of infectious diseases and the elimination of sanitary, occupational and other health hazards. Its recent accomplishments as outlined in a statement from the Office of the Surgeon General are reflected in the current health picture of the Army. The total disease admissions and death rates from troops have been extremely low; in fact, the current death rate from disease of only 0.6 per one thousand per annum is the lowest ever recorded in the history of the Army. Seasonal waves of mild influenza have occurred, but the death rate from this disease has been insignificant. Meningitis occurred almost in epidemic proportions during the past year, but due to early recognition of the disease and adequate treatment with sulfonamides the mortality was less than 5 per cent. as compared with a death rate of 38 per cent. in World War I. Venereal disease rates have been significantly lower than during the last war and are continuing to decline. The rates of certain insect-borne diseases and bacillary dysentery in some sections of the overseas theaters have been undesirably high where adequate control measures have been difficult to carry out under combat conditions, but the incidence from these diseases is steadily declining. There have been no reported cases of plague, cholera or yellow fever, and fewer than fifty cases of epidemic typhus have occurred with no deaths.

Specifically, among the accomplishments of the service during the past year were the following:

1. The Army Epidemiological Board and the ten commissions operating under the board increased the scope of their activities, particularly in overseas theaters, and made important contributions in the control of scrub typhus, meningococcal meningitis, measles, sandfly fever and respiratory diseases. Its Commission on Influenza has succeeded in developing a promising vaccine against influenza. Other commissions are making critical studies of infectious hepatitis, rheumatic fever, dengue fever and certain neurotropic virus diseases.

2. The prevention of insect-borne diseases among troops, particularly in combat areas, has been extensively studied and effective methods of control have been promulgated. The development and establishment of standard practices of application of DDT powder, aerosol insecticides and certain insect repellants have been effective in reducing the incidence of insect-borne diseases.

3. Days lost from duty because of venereal diseases have dropped from 1,278 per one thousand in 1940 to 400 per one thousand per annum and even lower non-effective rates are to be expected with the newer treatment methods utilizing sulfonamides and penicillin. In addition, during the past year over 100,000 civilians with venereal diseases have been inducted into the Army and successfully treated.

4. Sanitary engineering activities have ensured pure drinking water, adequate swimming and bathing facilities, waste and sewage disposal for troops; laboratories have been created and staffed with trained personnel; the Army industrial program has been expanded to ensure healthful working conditions and adequate treatment facilities for over 850,000 civilians employed in Army owned and operated arsenals, depots and plants; and training and assignment of nutrition officers has continued and studies are continually being made in cooperation with the Office of the Quartermaster General to improve existing rations.

THE BUDGET OF THE UNIVERSITY OF WISCONSIN

IT is announced that the budget of the University of Wisconsin for 1944–45 has been approved by the Board of Regents. It amounts to $7,105,288 for educational, science research and public service work during the fiscal year beginning on July 1.

Of this amount $4,277,144 is appropriated by the state. The university earns the remaining 40 per cent. of its budget from direct receipts, from federal grants or from gifts from business, industry, foundations and individuals.

The budget makes provision for the return of salary waivers, left over from depression days, to about a hundred faculty members in the higher salary ranks, whose salary waivers, first imposed in 1932, have never been restored. The waivers in the lower salary ranks were restored in 1937.

In addition, in order to comply with the requirement that civil service employees receive systematic increases on July 1 of each year, it will be necessary to request an appropriation of $60,344 from the State Emergency Board. This includes the appropriation for general operation, books and equipment; maintenance and operation of the physical plant; agricultural extension service; the agricultural experiment

station; the Psychiatric Institute; the State Laboratory of Hygiene; the State geologist; and the class instruction, correspondence study and general program of the University Extension Division.

Under the heading of research the budget provides for the study and investigation of special problems affecting the welfare of the people of Wisconsin, including studies in the prevention and cure of cancer, improvements in agricultural production and marketing, industrial research and the prevention and cure of diseases of animals and plants.

REPORT OF THE DIRECTOR OF THE CHICAGO NATURAL HISTORY MUSEUM

THE acting director of the Chicago Natural History Museum, Orr Goodson, gives in his annual report the following summary of the work of the museum:

The conditions existing in a nation whose efforts were almost totally directed to the demands of war naturally affected adversely the progress of the museum.

The inroads on the personnel continued at a steady pace, with a resulting decrease in the scope of museum activities, although every effort was made to operate all departments on a normal basis.

Under the policy adopted in 1942, to be continued for the duration of the war, there were no expeditions during 1943, and even local field work was held to a minimum.

Some new exhibits were prepared and installed, although not as many as would have been the case had the full staff been present.

Research slowed up in ratio to the shrinkage of the staff, and many projects that were in progress have been halted.

Seven men and two women were granted leave of absence in 1943 for service with the armed forces or other governmental agencies, bringing the total number of trustees, staff members and volunteer associates in service to 38.

The outstanding event of the year was the program on September 15 commemorating the fiftieth anniversary of the founding of the museum.

In conformity with the suggestion of Trustee Marshall Field and President Stanley Field, duly approved by the board of trustees, the name of the museum was officially changed on December 6, 1943, from Field Museum of Natural History to Chicago Natural History Museum.

Among contributions during the year toward the work of the museum $100,916 was received from Marshall Field, and from Stanley Field, president of the museum, $20,075.

The number of visitors to the museum during 1943 declined to 1,021,289 from 1,025,002 in 1942. Of this number all but 77,980 were admitted free.

Included in the report are résumés of the year's activities of the four scientific departments, anthropology, botany, geology and zoology; and of all the administrative and other divisions of the museum.

THE PACIFIC DIVISION OF THE AMERICAN PHYTOPATHOLOGICAL SOCIETY

THE twenty-seventh annual meeting of the Pacific Division of the American Phytopathological Society was held from June 26 to 28 at Oregon State College at Corvallis. Thirty-two members and twelve nonmembers from Oregon, Washington, California, Idaho, Nevada and Washington, D. C., were present, and twenty-two scientific papers were presented.

New diseases reported included the destructive blind-seed disease on rye grass caused by *Phialea temulenta* and described by Geo. W. Fischer. New methods for the control of plant disease included the disinfestation of old stakes for the control of bean rust on pole beans, as reported by J. A. Milbrath. Officers elected for 1945 are: *President,* B. L. Richards; *Vice-president,* H. R. McLarty; *Secretary-Treasurer,* Geo. W. Fischer; *Councilor,* L. D. Leach; and *Representative on the Council* of the Pacific Division of the American Association for the Advancement of Science, L. D. Leach.

C. E. YARWOOD,
Secretary-Treasurer

THE CHARLES MAYER FELLOWSHIPS

THE *Journal* of the American Medical Association reports that three of four fellowships entrusted to the committee on medical education of the New York Academy of Medicine have been awarded. The fellowships were provided by Charles Mayer of New York and consist of $2,000 each.

The recipients were Dr. Harry Goldblatt, associate director of the Institute of Pathology of the School of Medicine of Western Reserve University, and Dr. Philip Handler, associate in physiology and nutrition at the School of Medicine of Duke University, for work on "use of choline and other lipotropic factors in the prevention and treatment of fatty infiltration of the liver and hepatic insufficiency"; Dr. Richard Lewisohn, of the cancer research laboratory of the Mount Sinai Hospital, New York, for work on "the action of ingested choline, lecithin, methionine and inositol on precancerous lesions and disorders associated with neoplastic diseases"; and Dr. John R. Murlin, professor of physiology at the University of Rochester, for research on "the effects of riboflavin, certain amino acids and casein on the development and growth of cancer."

IN HONOR OF RALPH E. SMITH

A DINNER in honor of Professor Ralph E. Smith, who retired on June 30 as the oldest staff member in

years of service of the College of Agriculture, was given on June 13 by the staff of the Division of Plant Pathology of the University of California at Berkeley, some former students and long-time faculty associates. There were forty-two persons present. Dr. J. T. Barrett was toast master. After the dinner short talks were made by Professors R. L. Adams and E. B. Babcock, and by Stanley Rogers, who assisted Professor Smith during his early pioneer years of work in plant pathology in California. Professor E. O. Essig paid tribute to him for his contributions in the field of entomology and Dr. S. C. Brooks recalled the surroundings at Massachusetts State College, where Professor Smith graduated in 1894. A number of letters from former students were read. Dean C. B. Hutchison voiced the appreciation of the state and college for the valuable and able service rendered during the forty-one years that he had served the university. Professor Smith instituted in 1903 what is believed to be the first distinct Division of Plant Pathology in America. Dr. Max Gardner presented a billfold and wallet on behalf of his friends, to which Professor Smith responded.

SCIENTIFIC NOTES AND NEWS

FOREIGN members of the Royal Society, London, have been elected as follows: Dr. Oswald T. Avery, bacteriologist, member emeritus of the Rockefeller Institute for Medical Research, New York; Maurice Lugeon, professor of geology and director of the Geological Laboratory of the University of Lausanne; Dr. The Svedberg, professor of physical chemistry, and Dr. N. E. Svedelius, professor of botany at the University of Uppsala; and Dr. S. Timoshenko, professor of engineering mechanics at Stanford University.

THE King of England's birthday honors list includes the Order of Merit conferred on Sir Henry Dale, president of the Royal Society, and knighthood conferred on Dr. Alexander Fleming, professor of bacteriology at the University of London, and on Dr. H. W. Florey, professor of pathology at the University of Oxford, in recognition of their work on penicillin; and on Dr. Percival Hartley, director of Biological Standards of the British National Institute for Medical Research.

THE Albert Gold Medal "for distinguished merit in promoting arts, manufactures and commerce" of the Royal Society of Arts, London, has been conferred on Sir Henry Tizard, F.R.S., president of Magdalen College, Oxford, since 1933 chairman of the British Aeronautical Research Committee, who has been responsible for the scientific work in the development of aircraft in Great Britain.

THE Indian Association for the Cultivation of Science recently founded a gold medal in memory of Dr. Bimala Churn Law, "to be bestowed on a person who has made conspicuously important contributions to science including medicine." The first award of the medal has been made to Sir Henry Dale, president of the Royal Society.

THE Hickman Medal of the Royal Society of Medicine, London, has been awarded to Dr. Ralph M. Waters, since 1927 professor of anesthesia and director of the department of anesthesia of the Wisconsin General Hospital.

THE College of Physicians of Philadelphia has awarded the Alvarenga Prize to Dr. Gervase J. Connor, of the School of Medicine, Yale University, for his study entitled, "Anterior Cerebellar Function, an Analytical Study in Functional Localization in the Cerebellum in Dog and Monkey." This will be published in December in the Transactions and Studies of the College of Physicians. The Alvarenga Prize was established by the will of Pedro Francisco daCosta Alvarenga of Lisbon, Portugal, an associate fellow of the College of Physicians, "to be awarded annually by the College of Physicians on each anniversary of the death of the testator, July 14, 1883, to the author of the best memorial upon any branch of medicine which may be deemed worthy of the prize."

PHYSICISTS of Harvard University and of the Massachusetts Institute of Technology on July 9 joined in greeting Dr. Peter Kapitza, director of the Institute for Physics of the Academy of Sciences of the U.S.S.R., whose fiftieth birthday was being celebrated by the academy in Moscow. Their message offered "hearty congratulations from their American colleagues and sincere wishes for many years of continued fruitful work." Dr. Kapitza has been awarded the Order of Lenin "for outstanding scientific achievements in the sphere of physics."

COLONEL WILLIAM S. MIDDLETON, dean of the Medical School of the University of Wisconsin, who is on leave for the duration and who now is serving as chief consultant of medicine for the U. S. troops in the western theater of war, has been elected a fellow of the Royal College of Physicians, London.

CORNELL COLLEGE at its commencement conferred the doctorate of science on Dr. Harry Fletcher Lewis,

professor of organic chemistry at the Institute of Paper Chemistry of Lawrence College, Appleton, Wis. Dr. Lewis was from 1921 to 1928 professor of chemistry at Cornell College.

DR. REGINALD FITZ, lecturer on the history of medicine at the Harvard Medical School, has been chosen president-elect of the Massachusetts Medical Society.

DR. JOHN R. SCHENKEN, professor and head of the department of pathology and bacteriology of the School of Medicine of the Louisiana State University, has been elected president of the Louisiana Association of Pathologists. Dr. Emma S. Moss, assistant professor of pathology and bacteriology, has been elected secretary-treasurer.

THE retirement is announced of Dr. William F. Steve, professor of physics at the University of Wisconsin, with which he has been connected for thirty-seven years.

AT Cornell University Dr. C. H. Myers, professor of plant breeding, who has been associated with the university since 1912, has retired.

PROFESSOR T. Y. THOMAS, of the University of California at Los Angeles, has been appointed professor of mathematics and chairman of the department of Indiana University. As chairman he succeeds Professor K. P. Williams, who had served in that capacity since 1937. Professor Agnes E. Wells, who had been connected since 1919 with the university, since 1937 as professor of mathematics, retired on July 1.

DR. CHARLES A. MCDONALD, assistant professor of health, and Dr. Alex M. Burgess, assistant professor of biology, have been appointed professors of health and hygiene in the newly established department of medical sciences at Brown University.

AT the New York State Agricultural Experiment Station at Geneva, Dr. Charles L. Hamner, plant physiologist with the United States Department of Agriculture at Beltsville, Md., has been appointed assistant professor of pomology. He will engage in research on the maturity, storage and handling of nursery stocks. Robert F. Carlson, a recent graduate of the University of Minnesota, has been appointed investigator in pomology and will engage in plant propagation and nursery problems. Professor Arthur W. Clark, in charge of the inspection of commercial fertilizers and feedings stuffs in the division of chemistry, has leave of absence for six months.

LAWFORD H. FRY, railway engineer, has been appointed director of research of the Locomotive Institute.

DR. W. J. HALL, entomologist and director of the Citrus Estate of Mazoë of the Mazoë Citrus Experimental Station and superintendent of the British South Africa Company, has been appointed assistant director of the Imperial Institute of Entomology.

J. C. F. FRYER, director of the Plant Pathological Laboratory of the British Ministry of Agriculture at Harpenden, has been appointed to succeed the late Professor W. W. C. Topley as secretary of the Agricultural Research Council.

DR. S. LIVINGSTON SMITH, superintendent of the engineering department at the British National Physical Laboratory at Teddington, has been appointed director of research of the British Shipbuilding Research Association recently formed by the Shipbuilding Conference in close cooperation with the Department of Scientific and Industrial Research.

SIR STANLEY WOODWARK has been appointed president of the Royal Institute of Public Health and Hygiene, London.

DR. CHARLES P. BERKEY, professor emeritus of geology of Columbia University, is spending the summer in the western United States. Studies connected with projects of the U. S. Bureau of Reclamation illustrating the bearing of geological conditions on the design and construction of major engineering works are being reviewed for possible publication.

DR. HENRY S. SHARP, assistant professor of geology at Barnard College, Columbia University, is studying erosional surfaces in the Rocky Mountain region this summer.

DR. G. LOMBARD KELLY, who has been secretary of the Council on Medical Service and Public Relations of the American Medical Association under a six months leave granted by the School of Medicine at Augusta of the University of Georgia, returned on July 1 to the medical school as dean and professor of anatomy.

THE Desert Museum at Palm Springs, California, opened on October 16, 1943, and closed on May 7, 1944, for the summer. It will open again next October. Professor T. D. A. Cockerell and Mrs. Cockerell will spend the summer in Colorado. The museum had over 13,000 visitors from October to May, a large proportion of them soldiers.

THE Pacific Division of the American Association of Economic Entomologists held its twenty-ninth annual meeting at the University of California at Berkeley on June 27 and 28.

THE fiftieth summer meeting and twenty-sixth colloquium of the American Mathematical Society will be held on August 13 and 14 at Wellesley College, in conjunction with the summer meeting of the Mathematical Association of America and the Institute of Mathematical Statistics. Sessions of the society will

begin on Sunday morning, August 13, at nine o'clock and will continue through Monday. Sessions of the association will be held on Saturday. The twenty-sixth colloquium will consist of four lectures on selected topics in the theory of semi-groups by Professor Einar Hille, of Yale University. These lectures will be given at 9:00 A.M. and 2:00 P.M. on Sunday and Monday. At 3:15 P.M. on Sunday there will be an address "On the Composition of Algebraic Forms of Higher Degree" by Professor C. C. MacDuffee, of the University of Wisconsin. A joint session with the Institute of Mathematical Statistics will be held. The council will meet at 8:00 P.M. on Sunday. There will be a reception on Saturday evening and a dinner on Sunday evening, followed by a musical entertainment.

THE thirty-sixth annual meeting and war conference of the American Phytopathological Society will be held from December 9 to 11 at the Netherland-Plaza Hotel, Cincinnati. Dr. W. D. Valleau is chairman of the committee on general arrangements. Officers for 1944 are: *President,* J. J. Christensen, University Farm, St. Paul, Minn.; *Vice-president,* J. B. Kendrick, University Farm, Davis, Calif.; *Secretary,* C. C. Allison, the Ohio State University; *Treasurer,* R. M. Caldwell, Purdue University.

THE large collection of literature on galls and gall insects accumulated by Dr. Mel T. Cook has been presented by him to the library of the Ohio State University and has been catalogued and deposited in the botanical and zoological library.

THE *Journal* of the American Medical Association states that approval has been given to a contract between the Federal Office of Scientific Research and Development and Wayne University College of Medicine, Detroit, to conduct a study on the influence of the oral administration of sodium lactate solution. The Government will provide the sum of $7,500 to cover the cost of the project, which will be carried out under the direction of Dr. John W. Hirshfeld, assistant professor of surgery at the College of Medicine.

A CHAIR of social medicine has been founded at the University of Chile with a view to facilitating the application of the law of preventive medicine now in force.

Erratum: In the article by Dr. Carl E. Duffy entitled, "Interference between St. Louis Encephalitis Virus and Equine Encephalomyelitis Virus (Western Type) in the Chick Embryo," printed in SCIENCE for June 23, p. 51, the lines of the fourth sentence of the first paragraph were misplaced. This sentence should read: "Data obtained from the experiments reported here indicate that the 'interference phenomenon" is not limited to those viruses which are closely related, but that interference may occur between such unrelated viruses as St. Louis encephalitis and equine encephalomyelitis."

DISCUSSION

NEW VOLCANOES AND A NEW MOUNTAIN RANGE

AN article by Professor William H. Hobbs, of the University of Michigan, published in the issue of SCIENCE for April 14 under the above title has been given considerable publicity by a review and abstract headed, "New Mountain Range Rising. Central American Volcanic Threat," in the Scripps-Howard newspapers. Inasmuch as the original article as well as the review contains various misstatements of fact and erroneous conclusions, it should not remain unanswered in the pages of a scientific publication.

Omitting consideration of Dr. Hobbs's geological theories, his description of Central American topography is inaccurate and his inferences misleading. He seems to make no distinction between the long periods of geological time and the shorter intervals which concern the human race. There is no continuous mountain range along the Pacific Ocean beginning with Mexico and extending to Panama behind which lies a chain of volcanoes, nor is there any apparent evidence that there has been any material change of elevation along this coast for the last four centuries.

Sierra Madre del Sur is the name of a mountain range in Mexico and neither the name nor the range extends through Central America. The Central American volcanic chain consists mainly of isolated groups of volcanic cones situated not behind a rising mountain range but along the coastal hills fronting the Pacific shore. In Dr. Hobbs's list there are only two Central American volcanoes and of these only one, in El Salvador, shows signs of present activity. In addition to the break in the coastal range at Tehuantepec, there is a similar interval caused by the Gulf of Fonseca and again where the basin of Lake Nicaragua in a former geological age was a gulf with an outlet to the sea.

There are various high volcanic peaks in Guatemala. Santa Maria, near the Mexican frontier, opened a new vent some twenty years ago burying a neighboring town in a flow of hot mud. Fuego, twelve thousand

feet high, blew off its head in 1932 spreading ashes in a radius of fifty miles. Izalco in El Salvador commenced its career, as stated, in 1769 and has been more or less active since. San Miguel in the eastern part of El Salvador near the coast is apparently inactive. A large lava flow at its base is intersected by the line of International Railways of Central America. Other volcanic peaks around the Gulf of Fonseca include Cosegüina in western Nicaragua which in the last century had one of the most noted eruptions in history. Eastward in Nicaragua extends a line of coastal volcanoes, terminating with Momotombo at the western end of Lake Managua, which has been quietly smoking for many decades. Southeast of the lake the Nicaragua Railway crosses lava beds near Santiago, which, after many years of quiescence, started smoking in 1925 and for several years threw out great clouds of sulphurous gas, which extended many miles offshore and damaged coffee plantations on the nearby hills until an earthquake started cinder slides closing the vents in the crater and the smoke ceased. There are inactive craters near the western end of Lake Nicaragua and on islands in the lake, but no other considerable volcanic activity between Mexico and Costa Rica.

Dr. Hobbs's comments in reference to a Nicaragua Canal indicate lack of familiarity with the various projects studied previous to the construction of the Panama Canal. The line indicated on his map never received any serious consideration nor was there any plan for a lock at Managua. The route across Nicaragua has been surveyed many times without material variations and most recently between 1929 and 1932. It utilizes the lowest natural divide between the oceans throughout the Americas, only 155 feet above sea level between the Pacific and Lake Nicaragua. At its nearest point, this line is sixty miles distant from Managua.

In general there seems to be little connection between earthquakes and volcanic eruptions in Central America. The most destructive in the Caribbean area in recent years was that at Kingston, Jamaica, in 1906, an island which has only vestiges of former volcanic activity.

The possibility of earthquake damage to an Isthmian Canal was considered by various commissions, in preliminary studies. The fact that earthquakes have damaged Central American cities does not prove that massive structures like those at Panama necessarily would be affected. On the other hand there can be no guarantee against the occurrence of earthquakes at any site. As there is no sure way of predicting the occurrence or magnitude of earthquakes, their possibility must be accepted and designs made based on our present knowledge of earthquake resistant structures. The Managua earthquake destroyed more than a third of the city and killed an estimated 2,000 people. The buildings destroyed had stone or adobe walls unsupported against lateral shocks. Framed timber, steel and reinforced concrete structures were largely undamaged including a five-story building and a million-gallon reservoir. Proper engineering design now includes provision against lateral stresses due to earthquake shock. Such precautions have been taken in all design of important structures since the earthquake at San Francisco. Proximity to volcanoes is no reason for abandonment of construction activity, as is evidenced by the continued existence of the Port of Naples.

As concerns Dr. Hobbs's recommended canal at the Isthmus of Tehuantepec, this is a location which has never been seriously considered except for the ship railway proposed by Captain Eads about 1885. On this route there would be a long summit level at some seven hundred feet elevation and a doubtful water supply, two factors which eliminated it from consideration by the Isthmian Canal Commission. The author's recommendations amount in fact to a rejection of an impractical route in favor of another in the same category.

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COMPARATIVE STUDIES IN HUMAN BIOLOGY

SERIOUS reservations must be entered to certain points made by Professor Dice in his proposal for a program to study the problems of human biology by means of a concerted attack by the various disciplines concerned.[1] The following paragraph may be cited to give an example of the points to which exception is taken:

> The characters of man that are inherited include not only his anatomical features, but also his physiology and his psychology. For instance, each of the races of man is distinguished by certain physical characters, but it is recognized by anthropologists that many races also exhibit clearly marked peculiarities of physiology and psychology. It will of course be admitted that psychological and physiological characters are perhaps somewhat more subject to modification by the environment than are anatomical ones.[2]

Quite aside from the looseness with which the term "psychological" is employed—since there is no indication in statement or context whether an inborn neural system or learned behavior mechanisms are implied—it must be pointed out that it is simply not true that anthropologists recognize that races exhibit psychological or, to a lesser degree, physiological differences. The fact of the matter is that practically all anthro-

[1] SCIENCE, n.s., 99: 457–461, 1944.
[2] *Ibid.*, p. 458.

pologists not committed to the racist dogma hold exactly the opposite. There is no evidence to prove that the physical traits which mark off the races of man are correlated with psychological characters, whether this be of the order of intelligence or aptitude; on the other hand, there is good reason to believe that the gamut of human potentiality is run by every sizable group of men.

Professor Dice's use of the phrase "many races" is confusing, since one of the most difficult anthropological problems is to delimit the races of man. Even the three- or four-fold grouping most generally accepted is not broad enough to encompass all cases—as, for instance, the "hairy Ainu" of the island of Sakhalin, variously classified as Caucasoid or Mongoloid; or the peoples of Polynesia. One wonders, indeed, why the word "race" was introduced at all, since Professor Dice seems to be concerned with genetic studies of a restricted group of families. Many anthropologists to-day, as a matter of fact, tend to define a race as an aggregate of genetic lines rather than in the simple taxonomic terms of an earlier fashion which seems to be implicit in Professor Dice's usage. Or is Professor Dice using the word "race" as a synonym for "local group"?

The employment of the term "environment" perhaps reveals the principal source of Professor Dice's confusion. Does he mean the natural environment? Or does he mean culture? At one point he writes that "hereditary trends within families give a basis for studies of the variations in morphology, physiology and psychology that are produced by environmental influences." Later he considers the difficulty of "untangling in human affairs the complex interrelations of heredity and environment." But he also speaks of "physical environment" and of "social environment." These are two quite different things, holding different implications for the study of human biology. It is perfectly possible that high altitude imposes certain conditions on the developing human organism that cause it to have a distinctive character. But this is not a phenomenon of the same order as the food habits of a people, since these comprise a cultural fact and vary widely within the range of possibility presented by any given natural environment.

There is little question that a concerted attack on the problems of human biology, conceived and executed along the widest lines, is desirable. But such a study, made without a conceptual setting of the greatest clarity, and drawn in terms of the findings of all the various disciplines involved, will run the gravest danger of defeating its own ends and repeating errors of earlier days.

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ENZYMATIC SYNTHESIS OF CRYSTALLINE SUCROSE

THE bacterium *Pseudomonas saccharophila* Doudoroff was recently shown[1, 2] to contain a sucrose phosphorylase catalyzing the reaction

sucrose + inorganic phosphate → glucose-1-phosphate + fructose.

The reaction appeared to be reversible since when glucose-1-phosphate and fructose were added to a partially purified enzyme preparation inorganic phosphate and a carbohydrate having certain properties of sucrose were formed. The evidence, however, was not sufficient to establish the identity of the synthetic carbohydrate.

Additional experiments which we have recently completed justify the conclusion that the synthetic product is identical with natural sucrose. By the use of an invertase-free sucrose phosphorylase preparation, 2.5 g of the carbohydrate were obtained in crystalline form. The empirical formula, specific rotation, refractive indices and other optical properties, x-ray pattern, rate of acid hydrolysis and the reducing values before and after invertase or acid hydrolysis of the crystalline compound were all found to be the same as those of sucrose. In addition, the octaacetate derivative of the synthetic carbohydrate was shown to be identical with the corresponding sucrose derivative.

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PENICILLIN PRODUCTION

DURING a study of the growth of *Penicillium notatum* on sulfite waste liquor for penicillin production it was found that whereas lactose may or may not act as a nutrient for mold growth, it definitely serves as a preservative for penicillin. Assuming the same action for the large amounts of lactose added in the commercial production of penicillin on corn steep liquor, a more plentiful substitute preservative was sought.

We have found in preliminary parallel experiments using corn steep liquor that starch dextrin can be substituted for lactose to give equally high quantities of penicillin. The substitution of lactose by dextrin in the commercial production of penicillin might make possible a desirable increase in such production.

IRWIN A. PEARL
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APPLETON, WIS.

[1] M. Doudoroff, N. Kaplan and W. Z. Hassid, *Jour. Biol. Chem.*, 148: 67–75, 1943.
[2] M. Doudoroff, *Jour. Biol. Chem.*, 151: 351–361, 1943.

SCIENTIFIC BOOKS

DROSOPHILA MUTANTS

The Mutants of Drosophila melanogaster. By CALVIN B. BRIDGES. Completed and edited by Katherine S. Brehme. 257 pp. 128 text figures. 3 plates. Carnegie Institution of Washington. Publication 552. 1944. $2.50 in paper cover, $3.00, cloth binding.

MOST reviews and text-books of genetics are slightly out of date by the time they are published, seriously out of date five years hence, antiquated in ten and historical curiosities twenty years after publication. At least this used to be so before the war has applied a brake to the development of science. For two good reasons, the book under review will prove to be an exception. First, it embodies the records collected during a lifetime of work of one of the master builders of genetics. Second, it represents a type of research which, though by no means completed (a worth-while research seldom is), will hardly be pursued in the future by so many and so assiduously as it was in the past.

Between thirty and thirty-five years ago, T. H. Morgan pointed the way toward construction of genetic chromosome maps in *Drosophila melanogaster*. The realization of this task fell, however, to the lot, first of a small group of men usually referred to as "Morgan School," and later of an ever widening circle of geneticists the world over. Mutants in *Drosophila melanogaster* were being collected, studied, described, and their positions on chromosome maps determined in laboratories scattered from New York, Austin and Pasadena to Moscow, Peiping and Kyoto. But the undisputed leader in this work was C. B. Bridges. Assuredly more than a half of the multiple mutant stocks without which efficient work on chromosome mapping is impossible were "synthesized" by Bridges and distributed for the asking to all other laboratories. The records of published and unpublished data of all investigators were kept by Bridges on cards filled in by his peculiar shorthand notations. Since 1934 some of these data were from time to time systematized on pages of a mimeographed circular "Drosophila Information Service," issued by C. B. Bridges and M. Demerec at the Department of Genetics of the Carnegie Institution of Washington in Cold Spring Harbor. The issue of this circular which came out in 1938, only a few months before Bridges's death, contains the first draft of the book under review. Thanks to the initiative of M. Demerec, supported by T. H. Morgan for the colleagues of the late C. B. Bridges and by geneticists everywhere, K. S. Brehme was enabled to complete and edit the final work, which will stand as a memorial to a not very long but very useful life.

The first nine pages of the book are taken by introductory remarks and explanations of the symbols and abbreviations used. The main body of the work (pp. 10–236) contains descriptions of the mutants, arranged in alphabetic order. The balance of the book summarizes the contents by listing the mutants in the form of chromosome maps. For each mutant the following data are given when available: the symbol and the name of the mutant; the name of the discoverer and the date of the first finding; the location in a chromosome; bibliographic references; a very condensed description of the external and sometimes also of the anatomical, physiological, genetic and cytological characteristics; and, finally, an evaluation of the mutant according to the degree of its usefulness in the work of linkage studies. A kind of telegraphic style is resorted to in the presentation of the data, a specimen of which follows: "Hn^{r2}: Henna-recessive^2 Nordenskiöld, 33b9. DIS 7: 18 (1937) (called hn^3). Also referred to as #bu. Eye color darker than Hn^r in young flies. RK2." This can be translated as follows: a second recessive allele of the mutant gene "Henna" was found on February 9 of 1933 by Nordenskiöld; it was referred to under the symbol hn^3 on page 18 of the issue No. 7 of the "Drosophila Information Service" published in 1937; an alternative name "brunette" and the symbol "bu" derived from it were also used, and it is now proposed to suppress them; the eye color in this mutant is darker in young flies than in the mutant symbolized Hn^r; Henna-recessive^2 is a mutant fairly useful for linkage studies, and its locus in the chromosome is accurately known.

The text-figures (line drawings) illustrate the critical characters of some of the mutants; some of these figures have been excessively reduced during reproduction. The three plates show the external structure of the fly and maps of the salivary gland chromosomes (reprinted from the "Drosophila Information Service"). The book certainly can not be profitably read by non-specialists, but it is a veritable mine of information for a specialist. It describes mutants at 98 "most useful" and 43 "less useful" loci in the X-chromosome, 192 "most useful" and 36 "less useful" loci in the second, 114 "most useful" and 42 "less useful" in the third, and 7 "most useful" and 5 "less useful" loci in the fourth chromosome, a total of 537 loci. This is a much greater number of genes than is known in any other organism. It seems probable that this number includes a majority of the genes in *Drosophila melanogaster* which produce externally visible changes with appreciable frequencies, and that in the future the increase in the number of known genes of this sort will not be as fast as it was in Bridges's day.

TH. DOBZHANSKY

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PAIN

Proceedings of the Association for Research in Nervous and Mental Disease. Vol. 23. xii + 468 pp. Baltimore: Williams and Wilkins Company. 1942. $7.50.

THIS book is neither a treatise nor a summary, but a collection of papers dealing with those aspects of pain on which current work is most active; a representative cross-section of contemporary research on pain. In a noninvidious sense this represents the current fashion. It may be read profitably as an extension and as the current phase of the work included in the similar volume published in 1935, rather than as a new edition of this.

The experiences which can be collectively termed painful involve many factors, and are all things to all people. To the physiologist pain is a confusing barrage of nerve impulses in an intricate plexus of nervous elements, whose individual functioning even, he is only beginning to understand. The first few chapters deal with the analysis of this mechanism for conduction and coordination of pain-inducing impulses, and with arbitrary and controllable experimental methods for inducing pain on purpose. Not through any fault of the contributors, but because nobody yet knows the answers, one finds no specific interpretation of how a pain ending works, what happens to pain impulses at the synapses of the central nervous system, nor why some impulses in some pathways induce pain, and similar impulses in other pathways induce something else. If this is rather like Hamlet without the Prince, some of the other characters do so competent a job that the deficiency is not obtrusive.

To the suffering patient, on the other hand, the unfortunate but potential reader of the book, pain is chiefly something to be gotten rid of regardless of cause or consequences. The patient is represented in this book only by proxy, his physician appearing with a scientific power of attorney. For purposes of more rational analysis than the casual experience of pain affords, the neurologist breaks the subject down into two main divisions, pain as one among many sensations, like touch or hearing, both the causation and the effects of which must be understood to be adequately dealt with, and pain as an emotional experience of the patient, for whom it is incumbent on his doctor to devise a better pain-killer. When the patient says "My back aches," he may have something wrong with his back, but the ache is certainly in his brain, and the physician must then decide whether he can fix the patient's back, or whether he will be forced to cut off more or less of the patient's head. The middle portion of the book deals with the distribution of pain sources in the body, as an essential preliminary to deciding what to do about it, and with the bodily conditions which arouse pain. Final papers discuss the psychological factors involved in painful experience and the effect of pain in turn on other body functions. More of this material would have rounded out the subject.

Although pain is properly treated as one among many sensations, in one respect it is unique, and this is the factor which determines the approach of this book. While all sensation serves to give information concerning the environment (external or internal), pain is the one sensation whose particular function it is to give warning of threatened or actual damage. Nature has accordingly made this warning effective by the special feature of tying it to a central emotional state which is unpleasant and potentially violent, and to a system of responses which are in general designed to be protective. In view of this, the proper emphasis in dealing with other sensations is on making the sensation more emphatic, or on the more effective utilization of its apparatus. With regard to pain the chief emphasis is on interference with its effectiveness. These circumstances justify the special concern of clinicians with this particular sense, but also raise the question to what extent this normal and salutary response to injury should be interfered with.

The answer which one may infer is threefold. To some extent human intelligence may take over or at least assist in the avoidance of damage without more than a minor warning of its approach, a proposition which still receives little support from the perennial and careless resort to nostrums. Certainly to a greater extent the intelligence of the physician may be relied upon to do this; to the extent at least that once the initial pang has brought the patient under his management, other methods both of estimating the damage and of dealing with it may be more effective as well as more comfortable than to let nature take its course.

The third justification for interfering with pain is that the mechanism is prone to overact, not only to a non-utilitarian extent but actually to do further damage itself. This is illustrated in the discussion of the vicious cycle of itch, whose close relation to pain is noted, where scratching the itch may not only compound the injury but often increases the itch itself. It is more acutely recognized in those chapters dealing with the harmful effects on bodily function of extreme pain, in addition to the obvious conditions where pain, having given warning of danger, further pain can do little to correct it. Perhaps it is in the latter situation that a natural enthusiasm for relieving pain might overreach itself, by removing also the incentive to pro-

tective reaction, and this constitutes the chief urgency for further investigation not only of the pain mechanism itself, but of bodily responses to it.

It is still an open question whether human understanding of pain is sufficiently advanced to justify nature in further evolution, if not toward a happy faculty for self-hypnosis, at least in the direction of atrophy of the pain sense, before her recent experiments toward the increase of intelligence have had a more extensive try-out. This might inspire caution in neurologists who can now so successfully interfere with nature, as well as in readers of their researches who might be encouraged to invoke their more drastic expedients. In most fields of endeavor, technological advances tend to outrun discretion in their employment, and one may anticipate that by the time another volume on pain appears in this series, a section will be appropriate on the results of its abolition.

The discussions which follow each discourse should not be slighted by one who would get the full intimate flavor of the book.

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SOCIETIES AND MEETINGS

THE BRITISH SOCIETY FOR FREEDOM IN SCIENCE

MANY scientists have doubtless been disturbed by the growing tendency in this country to over-emphasize the socially utilitarian aspects of science, with resulting efforts to control and regiment all scientific activity, as exemplified most strikingly perhaps in the original Kilgore Bill. This tendency toward the "totalization" of science has grown to an even greater extent in Great Britain than here and has reached such proportions that a society has recently been formed, The Society for Freedom in Science, to combat the undesirable features of this tendency. The society feels that the time has now come to give as wide publicity as possible to its objects, and to enlist active support from scientists in all free countries, and in particular is desirous of enrolling members among the scientists of this country. The following is a statement of the objects of the society issued by the Committee of the Society for Freedom in Science in May, 1944.

I

Since about 1931 there has developed in Britain a school of thought which attacks the conception of science as a search for truth and denies the right to free research directed solely to that end. Three contentions underlie this movement:

(1) Science had its origin in efforts to satisfy the material needs and desires of ordinary human life.

(2) The legitimate purpose of science is to meet these material needs and desires on an expanding scale.

(3) Scientists can not be left free to choose their own subjects of research, but must submit to central planning so that their work will be specifically devoted to the satisfaction of human material needs and desires.

In this movement pure science is actually derided and compared in value with the solution of crossword puzzles.[1]

[1] J. D. Bernal, "The Social Function of Science." (Routledge, London, 1939). The reference to crossword puzzles is on page 97.

The effect of the movement was already apparent at the Leicester meeting of the British Association in 1933. The association's new outlook was reflected in Sir Frederick Gowland Hopkins's presidential address. As he said himself, "You may feel that throughout this address I have dwelt exclusively on the material benefits of science to the neglect of its cultural value." The movement first began to become really powerful in 1936, when the economist, Sir Josiah Stamp (later Lord Stamp), gave the presidential address to the British Association at Blackpool. For some years it looked as though the case of those who believe in pure science and freedom in science would go by default, through their continued neglect to state their own point of view. Professor J. D. Bernal's book, "The Social Function of Science" (1939), became a keystone of the movement against free science, which allied itself with Marxian politics. Certain scientific journalists joined the movement and spread its propaganda. The Association of Scientific Workers adopted the movement as a part of its policy, and has worked energetically on its behalf ever since, both privately and in public. Much publicity has been given to some of the meetings of the association, and the popular press has reported its deliberations as though they represented the voice of the general body of scientists.

In 1938 the British Association founded a new division, called "The Division for the Social and International Relations of Science," in which the voices of those who are opposed to pure science and to freedom in science have been particularly prominent. At a large and much-publicized meeting held at the Royal Institution, London, in September, 1941, the new movement reached the peak of its intensity. Pure science was repeatedly derided, speaker after speaker asking sarcastically whether applied science were "impure"; and some of the speeches were political and deficient in objective argument. No one was given the opportunity to speak during the three days of the

conference except those previously invited by the organizers, and only two voices were raised against the prevailing trend—those of Professor A. V. Hill and Professor M. Born.

II

For several years nothing was done to oppose the new movement apart from the publication of a few articles and the making of an occasional speech. Many scientists were disquieted, but not alarmed. There was little realization that the power of influencing public opinion was tending to pass from the hands of those who believe in pure science and freedom in science into the hands of those who do not. It was not until 1939 that a comprehensive and considered reply was made, in the form of Professor M. Polanyi's "Rights and Duties of Science,"[2] in which Professor Bernal's book was examined and the arguments contained in it answered.

In 1940 a letter was sent to 49 scientists, suggesting the formation of a new society to promote the causes of pure science and of freedom in science. A group of thirty was thus formed, and this became the nucleus of the Society for Freedom in Science. It may be remarked that conditions can be imagined under which the attempt would be made to foster pure science, while freedom of choice in subjects of research would be denied to the individual scientist. Nevertheless, it is a fact of experience that those who value pure science highly are commonly those who also value freedom in science, and thus it came about that a small natural group of like-minded people was formed.

A few of the original members who were seriously alarmed by the trend of events in the scientific world met together to draft a document which would draw attention to what was happening and would form a basis for a larger society consisting of those scientists who were willing to support a movement for the defence of scientific freedom. This document was circulated in May and June, 1941. It contained the following five propositions:

(1) The increase of knowledge by scientific research of all kinds and the maintenance and spread of scientific culture have an independent and primary human value.

(2) Science can only flourish and therefore can only confer the maximum cultural and practical benefits on society when research is conducted in an atmosphere of freedom.

(3) Scientific life should be autonomous and not subject to outside control in the appointment of personnel or in the allocation of the funds assigned by society to science.

(4) The conditions of appointment of research workers at universities should give them freedom to choose their own problems within their subjects and to work separately or in collaboration as they may prefer. Controlled teamwork, essential for some problems, is out of place in others. Some people work best singly, others in teams, and provision should be made for both types.

(5) Scientists in countries not under dictatorial rule should cooperate to maintain the freedom necessary for effective work and to help fellow-scientists in all parts of the world to maintain or secure this freedom.

The Society for Freedom in Science is an informal body, with no rules and no regular subscription. The first committee was self-appointed and provisional, but elections have since been held and the present committee consists of the following: Dr. J. R. Baker, Professor V. H. Blackman, F.R.S., Mr. R. Brown, Professor J. A. Crowther, Professor M. Polanyi, F.R.S., Dr. L. E. Sutton, Professor A. G. Tansley, F.R.S., and Professor A. E. Trueman, F.R.S. The society has no official president.

A general meeting was held in London on July 2, 1942, but the society's business has mainly been transacted by correspondence and by the circulation of typewritten and printed papers. The present membership is 134. Although a few reside so far away as Alberta, Uganda and Iraq, and quite a number are connected with the applications of science to practical affairs, the great majority are members of the scientific staffs of universities in Britain. (An attempt to found a sister-society in the U. S. A. broke down because almost at once that country became absorbed in the consequences of the Pearl Harbor attack.) The committee has made connection with like-minded people attached to other intellectual pursuits, by drawing into membership several distinguished philosophers and historians, including Sir Ernest Barker and Professor Sir J. H. Clapham, P.B.A., who form a valuable link with a wider field of ideas. The society is non-political in the sense of including members who are socialists, liberals and conservatives, but it is openly opposed to totalitarianism of all kinds in science.

III

The main function of the society is to form a solid body of opinion ready to present the case for freedom if the threat to suppress scientific liberties should develop dangerously in the period of reconstruction after the war. Those who lay all the stress on the applications of science and consider that research should be centrally planned are not only highly organized and extremely active, but also influential in certain political circles. Only a state of preparedness can make it certain that the case for freedom in science will get a proper hearing if and when such a crisis arises.

[2] M. Polanyi, "Rights and Duties of Science." (Manchester School of Economics and Social Studies, October, 1939, p. 175.)

Meanwhile, the society develops its case by fostering the publication of books, articles and letters on the subject, and circulating some of these among its members and among others who seem likely to be interested. The question whether scientific research flourishes best under freedom or under central planning is only part of the wider subject of scientific method in a broad sense. The society supports the publication of articles on scientific method and on the philosophy of science, so far as these bear upon the subjects in which it is interested.

It is believed to be better to concentrate on limited objectives rather than to make feeble efforts over too wide a range. The securing of freedom in the choice of subjects of research for members of the staffs of universities is considered one of the most essential of these limited objectives. In many university departments there is already considerable freedom, even in universities whos statutes do not grant it. In such cases the society wishes to conserve what it considers good, against the whole trend of totalitarianism which is so influential in the modern world. In some departments, however, the newcomer is expected to join a team already engaged on a definite scheme of research. In many cases newcomers are well fitted and perfectly willing to follow such a course and their freedom is therefore not compromised. But room should always be found in a department for independent investigation on any subject within the scope of the department by members of the staff or by postgraduate students who desire to choose their own subjects and are qualified to pursue them. It is recognized, of course, that freedom must necessarily be limited by the funds and apparatus available in the department in which the research is done.

It is felt that if freedom can be attained and maintained in universities, the effect of that freedom will be felt over a much wider field. It is held to be essential to the well-being and progress of science at large that those who desire and are qualified to undertake independent research should be given opportunity to do so.

The society fully recognizes that owing to the complexity of modern science, organized team-work is often necessary; and it is inevitable that a considerable proportion of the funds assigned to research should go to the support of such work. But substantial sums should also be made available for qualified individual investigators, whose independent discoveries often lead to the most important advances in knowledge and in technique. It goes almost without saying that the society is strongly in favor of the spontaneous collaboration which so often arises from the free discussion of their problems and interests by those trained in different branches of science. This is probably the most fruitful of all kinds of collaboration.

It is no part of the society's policy to insist that every man or woman who has been appointed to a research post should be allowed, at the expense of the community, to occupy himself or herself indefinitely with trivial investigations. This however is a difficult question, because the opinions of scientists may differ as to what is trivial and what is not. It may be suggested that the pressure of the public opinion of his colleagues is likely to be sufficient to deter a scientist from the indefinite pursuit of researches which are regarded by those colleagues as of little importance in the advancement of science. In so personal a matter as independent research a large amount of individual freedom is essential, but the individual investigator ought not to escape, and in fact can not ultimately escape, the judgment of his colleagues. He must be given the maximum freedom possible, and it is suggested that no pressure should be put upon him except in the most extreme cases, other than the inevitable moral pressure of the opinion of his colleagues; and scientists should recollect that young colleagues are often as likely to have useful opinions on scientific values as their elders.

IV

It is thought that the society has already had considerable influence. The totalitarian view does not now go unanswered, whether in conversation or in print, as it so often did in the thirties. There is an awareness of the existence of strongly held opinions contrary to the totalitarian view. The society has been a factor in the production of books, of articles and letters in journals and of addresses, in which the case for free science and pure science has been boldly stated and the totalitarian arguments contested. Many of the printed papers upholding the cause of free science have received a wide circulation through the society. In the present temper of the scientific world it is doubtful whether such a one-sided meeting as that of the Division for the Social and International Relations of Science held in September, 1941, could be held again.

Membership of the society is open to every established scientist who is in substantial agreement with the five propositions given above. It is thought desirable to increase the membership of the society, so that the movement for freedom in science may have the most influential backing possible, particularly if a crisis should develop. Now that the end of the war no longer seems remote, it is necessary to be prepared to remind the community of the non-material ends to which science, as one part of the search for truth, must be directed; because material ends are bound to

appear of great importance in the period of reconstruction. Those who wish to join the society should complete an enrolment form and send it to the Hon. Secretary, Dr. J. R. Baker, University Museum, Oxford. Members are under no obligation except that of supporting the cause of freedom in science. It is assumed that all members will fight vigorously for this cause if an immediate threat develops.

My own connection with the society started about a year ago as a result of correspondence initiated by its secretary, Dr. John R. Baker, who had seen the part of my presidential address to the American Physical Society published in SCIENCE of February 12, 1943, in which I expressed concern over the growing tendency toward totalization of science. Dr. Baker has asked me to serve as the go-between during the initial stages of enrolment of members in this country; enrolment blanks may be obtained by application to me.

It is pertinent to mention that a book by Dr. Baker is shortly to be issued by Macmillan called "Science and the Planned State."

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SPECIAL ARTICLES

THE CORRELATION OF THE INSULIN CONTENT AND THE HISTOLOGICAL PICTURE OF THE PANCREAS AT INTERVALS AFTER THE ADMINISTRATION OF ALLOXAN[1]

IN 1937, Jacobs[2] showed that the intravenous injection of alloxan produced fatal hypoglycemia in rabbits. He did not report any histological studies. In 1943, Dunn, Sheehan and McLetchie[3] confirmed the hypoglycemic effect of alloxan in rabbits and found that it produced a selective necrosis of the islets of Langerhans. Bailey and Bailey[4] were the first to show that if animals were kept alive during the hypoglycemic phase by glucose administration, extreme hyperglycemia subsequently developed. Within a short time, this work has been confirmed and extended by a number of investigators (see E. P. Joslin, 1944).[5]

The way in which alloxan affects carbohydrate metabolism, particularly the means by which it induces a profound temporary hypoglycemia before it causes a severe and prolonged hyperglycemia, is a problem of considerable interest. Two hypotheses have been advanced to explain this action: (1) that alloxan overstimulates the islet cells, causing excessive liberation of insulin and subsequent death of islets perhaps from exhaustion, and (2) that alloxan primarily destroys islet cells and that there is a slow release of insulin from the dying or dead cells which is sufficient to account for the hypoglycemia (Hughes, Ware and Young).[6]

It was thought that experiments in which the insulin content of the pancreas was determined at different times after the administration of alloxan and correlated with the histological picture in the islets at these times might provide information to settle this point. An investigation of this kind has not previously been published, although Goldner and Gomori[7] have reported a low insulin content of the pancreas in two dogs after treatment with alloxan.

Experiments on Rats. Female Wistar rats (about 210 grams each) were used. These were divided into five groups and four of these were injected subcutaneously with an aqueous solution of 350 milligrams of alloxan per kilogram in 4 equal doses at 15 minute intervals. The insulin content of the pancreas was determined by the mouse method of assay, using from 200 to 240 mice for each solution (Table 1).

TABLE 1

Number of rats	Time after alloxan	Blood sugar	Insulin per group of 10 rats
	(hours)	(mgms. per cent.)	(units)
26	0	92	21.2
12	1.5	215	21.1
13	3.0	293	18.7
14	7.0	100	16.0
13	48.0	264	0.89

For each group of rats upon which insulin assays were made, 5 similarly treated rats were used for histological studies. In these the islets showed the following changes. At 1.5 hours after alloxan the islet cells bordering capillaries showed ragged disintegrating edges and the capillary spaces were widened; at 3 hours these changes were more pronounced and there were many pycnotic nuclei; at 7 hours there was a general disintegration of islet structure with most of the cells necrotic; and at 48 hours, although super-

[1] This research has been supported in part by a grant from the Banting Research Foundation.

[2] H. R. Jacobs, *Proc. Soc. Exp. Biol. and Med.*, 37: 407, 1937.

[3] J. S. Dunn, H. L. Sheehan and N. G. B. McLetchie, *Lancet*, 244: 484, 1943.

[4] C. C. Bailey and O. T. Bailey, *Jour. Am. Med. Asn.*, 122: 1165, 1943.

[5] E. P. Joslin, *New Eng. Jour. Med.*, 230: 425, 1944.

[6] H. H. Hughes, L. L. Ware and F. G. Young, *Lancet*, 246: 148, 1944.

[7] M. G. Goldner and G. Gomori, *Jour. Am. Med. Asn.*, 124: 802, 1944.

ficially the islet structure seemed greatly restored, many of the regenerated cells were fibroblasts.

Experiments on Dogs. The amount of insulin in the pancreas of dogs was estimated at different times after the administration of 150 milligrams alloxan per kilogram. D 27 was given the full amount in a single injection. The other four animals received 4 equal doses at 15-minute intervals. Sections were taken from different parts of each pancreas and the remainder used for the insulin assay. The values in Table 2 were calculated as units per gram of total pancreas.

TABLE 2*

Dog number	Time after alloxan	Blood sugar	Insulin per gram of total pancreas
	(hours)	(mgms. per cent.)	(units)
D 21	0	80	2.5
D 22	2	340	3.5
D 23	4	195	2.2
D 24	8	45	3.2
D 25	24	278	none detectable
D 27	36	40	0.16

* The blood sugars reported in Table 2 are the ones obtained immediately before the termination of the experiment. Blood sugars, however, were determined at frequent intervals throughout the experiment on each dog. With the exception of D 27 there was the initial hyperglycemia reported by other workers. In D 24 and D 25 hypoglycemic levels were reached in 8 hours. D 27 showed no increase in blood sugar throughout the whole experiment and in 10 hours the blood sugar had fallen to 40 milligrams. The animal had convulsions which continued in spite of intravenous glucose until it was sacrificed.

The histological findings in the islet cells of the above dogs were as follows: in D 2 the capillary spaces were widened; the islet cells were not as regularly arranged as normally; some of the nuclei were pycnotic and many cells appeared shrunken. In D 23 pycnotic nuclei were more frequent and the cell cords were greatly disorganized. In D 24 most of the islet cells were necrotic with their nuclei failing to stain blue with hematoxylin. Small hemorrhages were seen in the necrotic tissue. In D 25 the islets were shrunken and difficult to detect. Their internal structure was disorganized and dead cells were seen in them. The smaller veins throughout the pancreas showed many marginal neutrophiles and the epithelium of many of the smaller ducts was vacuolated. In D 27 the islets seemed to be fewer and smaller than normal and there was considerable variation in the histological picture they presented. Few normal cells were seen in them.

The experiments on both the rats and dogs support the view that alloxan quickly destroys islet cells and that the insulin content of the pancreas does not fall substantially until some time after most of the islet cells are dead. The subsequent release of insulin which presumably lowers the blood sugar can not then be in the nature of a secretory phenomenon because it occurs when the islet cells are dead; it must, therefore, be a process wherein the insulin content of the islets is leached from the dead cells into the blood stream.

Further evidence that the hypoglycemic effect of alloxan is due primarily to its action on the pancreas rather than upon the liver or other tissues is provided by the following experiment in which alloxan failed to exert a hypoglycemic effect in animals containing little or no islet tissue.

Alloxan was given as described above to 2 depancreatized dogs, to 2 dogs that had been made diabetic by previous treatment with alloxan and to a normal dog. The blood sugars of the diabetic dogs were controlled by an injection of protamine zinc insulin given 18 hours previous to alloxan. In both types of diabetic dogs receiving alloxan there was no reduction in blood sugar. This is in direct contrast to the result in this and many other normal dogs in which hypoglycemia occurred in 5 to 6 hours after alloxan.

Summary and Conclusions. Experiments are reported in which insulin assays and histological studies were made on the pancreases of rats and dogs at different times after the administration of alloxan. It was found that the insulin content of the pancreas did not fall appreciably until after most islet cells were found by histological examination, to be dead. A further experiment showed that alloxan did not exert a hypoglycemic effect in depancreatized dogs and dogs previously made diabetic with alloxan.

These experiments indicate that alloxan causes hypoglycemia because it kills islet cells and so allows their insulin content to be leached out into the blood stream. It appears most unlikely that it exerts its hypoglycemic effect by stimulating islet cell secretion because most of the islet cells are dead when the hypoglycemic phase occurs.

The authors are indebted to Professor C. H. Best for suggesting these problems and for his advice and help during the investigations.

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THE CREATINE AND CREATININE EXCRETION OF NORMAL ADULT MALES[1,2]

IT is the purpose of this report to subjoin the data on the creatine and creatinine excretion of 30 normal human subjects which were collected from our investigations in human amino acid deficiencies to the existing and overwhelming factual evidence which indicates

[1] From the Department of Pediatrics, Johns Hopkins University, Baltimore, Md.

[2] Aided by grants from the Rockefeller Foundation, E. Merck and Company, Eli Lilly and Company, E. R. Squibb and Sons.

a long overdue revision of the prevalent statements; that, in a given individual, the elimination of creatinine is constant from day to day and that creatine is not present in the urine of the normal adult male.

Although the general validity of Folin's Law of constant daily creatinine has been generally accepted the constancy which it asserts must be allowed to be something short of absolute, as is indicated by the data upon which it is based.[3] In an extended study on 33 normal male and female subjects on hospital fare, Wang[4] found fluctuations of 10 to 25 per cent. of the individual creatinine output to be of common occurrence. In our experiments with 30 normal subjects studied for 38 to 60 days under normal and experimental dietary conditions individual daily variations of 10 to 25 per cent. of the total creatinine were also observed. These observations would seem to indicate that the irregularities in creatinine excretion are greater than heretofore presumed and that variations in creatinine output are not necessarily indicative of inaccurate 24-hour collections.

The truly remarkable feature of the creatinine excretion is its relative constancy under tremendous variations in protein intake. In this we have been able to amply confirm the findings of Folin, for, in subjects whose protein intake was changed from 13 to 14 g N/day to 1.5 g N/day, the daily creatinine variation was found to be no greater than that observed at normal protein intake levels. It is noteworthy, in this connection, that Benedict[5] observed a creatinine variation of only 1.40 to 0.86 g/day in the 30-day fasting man which is not greater than that found in normal well-fed individuals.

The failure of the earlier workers to observe creatinuria in the normal adult male is difficult to explain except that it might have been due in part to the lack of adequate methods and equipment which will be discussed below. In Table 1 are compiled summaries of the data from the investigations of others and ourselves. It is clear from this evidence that creatinuria occurs in all age groups of males so far investigated and that the observed values fall well within those found for women. Hobson[6] found, moreover, that a high carbohydrate intake increased the creatinuria; whereas, the amount of physical exercise was without effect. In our studies the creatine and creatinine output were measured daily for periods of 38 to 60 days and absence of creatine from the urine was sporadic and never extended for more than a single day in any of the subjects studied. Since meats, milk and cereal proteins were excluded from these diets, the regimen is considered creatine poor. On the basis of these findings, creatinuria in the adult male can not be considered symptomatic of starvation or hyperthyroidism, unless it be in excess of the levels recorded in Table 1.

TABLE 1

CREATINURIA IN NORMAL ADULT MALES

Investigator	Age group studied	Age limit of creatinuria	No. of subjects studied	No. of subjects with creatinuria	Creatine excreted/day	Diet
	yrs.	yrs.			mg	
Folin and Denis[12] .	8–17	17	3	3	90–150	Normal
Rose[13] ...	1–19	13	19	13	25.3/100cc	Normal
Light and Warren[14]	14–19	19	81	35	17–117	Normal
Taylor and Chew[10]	20–34	34	15	14	0–196	Normal
Djen and Platt[11] .	21–58	58	148	108	0–428/1.	Chinese diet
Hobson[6] ..	19–30	30	96	97	92–1200	Normal; carbohydrate varied
Wang[4] ...	20–55	55	15	11	0–200	Normal
Authors .	19–35	35	31	31*	0–796	Various
	19–35	35	14	14	184–352	Normal
	19–25	25	9	9	202–358	Vegetables, fat and carbohydrate
	19–25	25	8	8	17–796	Casein digest, fats, vegetables, carbohydrates
	19–23 (females)	23	4	4	61–354	Casein digest, fats, vegetables, carbohydrates

* Based on 850 individual determinations.

In another series of experiments on 4 adult males, we found that the ingestion of 6 to 10 gms arginine hydrochloride daily in addition to the normal diet for periods of one month or more failed to affect the creatinine or creatine levels in the urine.

EXPERIMENTAL

Collection of urine. Complete 24-hour specimens were collected in brown bottles containing 50 cc 15 per cent. HCl and 1 cc 10 per cent. alcoholic thymol and diluted to a uniform 2-liter volume (pH 4–5) before removing samples.

Creatinine Determinations. The method of Folin[7] was adapted to the Klett-Summerson photoelectric colorimeter. The color measurement was made with the S-54 filter and a solution containing 1.6102 mg/cc creatinine zinc chloride (C. P. Pfanstiehl, 23.3 per cent. N found) in 0.1 N HCl equivalent to 1 mgm/cc creatinine served as the standard. The color reaction conforms to Beer's Law from 0.5 to 3.0 mgm creatinine/100 cc. It was found that 1 cc samples of urine give suitable readings. Care was taken that the picric acid conformed to the standards of purity established by Folin and Doisy[8] (20 cc saturated picric acid solution diluted to 100 cc with water served as the reagent blank). A series of precision tests revealed the

[3] O. Folin, *Am. Jour. Physiol.*, 13: 45–117, 1905.
[4] E. Wang, *Acta Med. Scand.*, Suppl. 105, 1939.
[5] F. G. Benedict, "A Study of Prolonged Fasting," Carnegie Inst. of Washington, Washington, D. C., 1915.
[6] W. Hobson, *Biochem. Jour.*, 33: 1425, 1939.
[7] O. Folin, *Jour. Biol. Chem.*, 17: 469, 1914.

optical colorimeter technique to introduce an error of ±10 per cent. in the final result.

Creatine Determination. The conversion of creatine to creatinine was accomplished by the autoclave method of Folin.[7] Inasmuch as the creatine value is obtained by difference of the preformed and total creatinine, it was considered advisable to check the amount of creatinine destroyed and the extent of creating conversion effected by this procedure. The decomposition of creatinine was studied by submitting 1 cc samples of the creatinine zinc chloride standard to the Folin autoclave technique for varying periods of time (Table 2). A similar experiment with creatinine (C. P. Pfanstiehl) indicated an equal amount of destruction. These colorimetric findings were checked with a gravimetric procedure in which the creatinine was isolated and weighed as the flavianate in samples before and after autoclaving with 3 cc 10 per cent. flavianic acid for 20 minutes at 121° C. Three 50 mg samples in 10 cc which were not autoclaved yielded an average 191.4 mg creatinine flavianate or 50.2 mg creatinine; three autoclaved samples yielded 178.4 mg creatinine flavianate or 47.1 mg creatinine. This indicates a 6 per cent. decomposition of creatinine under the conditions of the method.

The efficacy of the creatinine conversion was tested by autoclaving 1 cc samples of a 0.1 N HCl solution containing 1 mg/cc creatine (C. P. Pfanstiehl, 32.0 per cent. N found) with 20 cc saturated picric acid solution. The extent of conversion was estimated colorimetrically (Table 2). In our experiments with the 3-hour boiling procedure of Folin[9] 83.5 to 86 per cent. creatine was found as creatinine. Due to the destruction of creatinine, it is obviously not possible to realize a complete conversion of creatine by this method.

TABLE 2

THE DECOMPOSITION OF CREATININE AND CONVERSION OF CREATINE TO CREATININE BY AUTOCLAVING AT 121° C.

Autoclaving time minutes	Creatinine decomposition Per cent.	Creatine conversion to creatinine Per cent.
10	7	67.5
20	8	86.5
40	9	92.6
60	9	93.0

Since the creatine value for adult males is normally about 10 per cent. of the creatinine output, it is understandable that if a correction is not made for the 8 to 9 per cent. creatinine decomposition incurred a low or no creatine output will be observed. It was found convenient to effect this correction by obtaining the creatine value as the difference of the total creatinine and the preformed creatinine of 1 cc samples which were simultaneously autoclaved with and without picric acid. The value so obtained is further corrected for the conversion of creatine into creatinine by the factor 1.16. The final formula for calculating creatine becomes:

$$\text{Creatine mg/day} = \frac{R_1 - R_2}{R_3} \times 1.16 \times \text{urine volume of specimen}$$

Where R_1 = total creatinine reading of 1 cc urine autoclaved with 20 cc saturated picric acid.

R_2 = preformed creatinine reading of 1 cc urine autoclaved without picric acid.

R_3 = reading of 1 cc of autoclaved standard containing 1 mg creatinine in 0.1 N HCl.

A comparison of the creatine excretion of normal adult males from 23 to 25 years of age on normal diets as determined by the Folin method and our modification showed our values to be 30 to 50 per cent. higher.

Inasmuch as creatinuria in the adult male has been consistently observed by others[6, 10, 11] who used the original Folin procedure, our creatinuria findings can not be considered specifically due to our technique, but we feel that a more accurate result is attainable by our modification.

SUMMARY

(1) It has been observed that the creatinine excretion of males and females is not an absolute value for the individual and is not influenced appreciably by the level of protein intake.

(2) Creatinuria in the adult male is a normal process and not a feminine or prepuberal male characteristic.

(3) A simple modification of the Folin method for determining creatine is described which reveals considerable quantities of creatine that may be present in urine but not detectable by the Folin technique.

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CORN OIL AND BUTTERFAT ESSENTIALLY EQUAL IN GROWTH-PROMOTING VALUE

THE Committee on Fats of the Food and Nutrition Board, National Research Council, has recently published a report on margarine.[1] In an evaluation of the relative nutritive value of different fats it comes to the conclusion that: "There is not complete agreement in the results from different laboratories as to the comparative value of different fats fed at the same level. Furthermore, with repeated experiments the results are not always the same in a given laboratory. Differences between fats will be found at one time which are statistically significant but which are not reproducible at another time with a new group of rats and a new batch of the same kind of fat."

[8] O. Folin and E. A. Doisy, *Jour. Biol. Chem.*, 28: 349, 1917.

[9] O. Folin, *Zt. f. Physiol. Chem.*, 41: 223, 1904.

[10] F. H. L. Taylor and W. B. Chew, *Am. Jour. Med. Sci.*, 191: 256, 1936.

[11] L. G. Djen and B. S. Platt, *Trans. Cong. Far East Assoc. Trop. Med., 9th Cong.*, 1: 379, 1934.

[12] O. Folin and W. Denis, *Jour. Biol. Chem.*, 11: 253, 1912.

[13] W. C. Rose, *Jour. Biol. Chem.*, 10: 265, 1911.

[14] A. B. Light and C. R. Warren, *Jour. Biol. Chem.*, 104: 121, 1934.

[1] Reprint and Circular Series, No. 118. August, 1943.

Wisconsin investigators have claimed the superiority for growth of butterfat over vegetable oils when the sole carbohydrate in the diet was lactose. They state that the younger the experimental animals, the greater are the differences obtained.[2] These conclusions were reached from a series of studies conducted with rats fed *ad libitum*.

Deuel and co-workers[3] repeated the comparison, but their results did not confirm the findings of the above mentioned investigators. They contend that the disagreement of results was due to the fact that weanling rats prefer a butter flavor and will therefore consume more of such a diet.

In this study, baby rats were paired according to litter, sex and weight. One group was completely weaned at the age of one week and another at two weeks. These two groups were force- and pair-fed with the aid of a medical syringe whose needle was modified to suit the purpose. They were fed up to the age of three weeks an artificial liquid milk simulating in composition that of the rat. One member of each pair received 15 per cent. butterfat (obtained from the university creamery), while the other received 15 per cent. corn oil (Mazola).[4]

After weaning age, the rats received a synthetic solid milk diet whose composition was as follows:

60	parts	ether extracted skim milk powder
7	"	casein
6	"	salt mixture
27	"	butterfat or corn oil

This ration was amply supplemented with thiamin hydrochloride, riboflavin, pyridoxine hydrochloride, calcium pantothenate, choline chloride, niacinamide, ascorbic acid, calciferol, carotene and alpha-tocopherol.

An analysis of the gains in body weight, as well as of the chemical composition of the carcasses, was made the basis of comparison between butterfat and corn oil. The average results obtained are shown in Table 1.

TABLE 1

SUMMARY OF PAIRED-FEEDING TESTS

	Weaned at one week*			Weaned at two weeks†		
	Butterfat	Corn oil	Diff./s.d. = "z"	Butterfat	Corn oil	Diff./s.d. = "z"
Body gains at 9 weeks, gms‡	133.7	137.5	0.63	132.8	136.8	0.45
Body lengths at 9 weeks, mm	187.2	188.9	0.50	190.1	187.9	0.94
Carcass analyses:						
Dry substance, per cent.	37.79	37.12	0.39	36.92	35.74	0.69
Ether extract, per cent.	13.79	12.26	0.59	13.03	10.02	1.65
Gross energy, cal/gm	2412.6	2339.6	0.39	2363.3	2219.4	1.00
T.N. × 6.25, per cent.	18.67	19.03	0.38	19.05	19.51	0.73

* Eight pairs, three males and five females.
† Eight pairs, four males and four females.
‡ Body gains based on empty weights.

Statistical analysis of the data by Student's method for paired observations[5] did not show significant differences between the butterfat and corn oil groups with the exception of the ether extract and gross energy content of the carcasses in the rats weaned at the age of two weeks. This problem is being studied further.

TABLE 2

SUMMARY OF *ad libitum* FEEDING TESTS

	Experiment 1*		Experiment 2†	
	Butterfat	Corn oil	Butterfat	Corn oil
Body gains and standard error, gms‡	143.4 ± 2.72	169.8 ± 2.08	97.8 ± 2.89	91.0 ± 4.77
Food consumption and standard error, gms	361.4 ± 13.12	397.4 ± 6.71	198.0 ± 5.67	183.3 ± 7.49
Body length and standard error, mm	204.4 ± 2.01	215.2 ± 1.96	189.0 ± 1.29	182.7 ± 0.91

* Six males to each group. Three weeks experimental period.
† Five males to each group. Six weeks experimental period.
‡ Based on empty weights.

In a study involving *ad libitum* feeding with weanling rats, using the same synthetic solid milk diet, it was found that the rats fed corn oil made better gains and attained a greater body length than those fed butterfat. The food consumption, however, was likewise considerably greater. In all three instances, the differences were statistically significant. In a parallel

[2] R. K. Boutwell, R. P. Geyer, C. A. Elvehjem and E. B. Hart, *Jour. Dairy Sci.*, 26: 429–437, 1943.

[3] SCIENCE, 98: 139–140, 1943.

[4] In all cases when the rats were weaned at the age of one week, bilateral cataracts occurred. These were noticed as soon as the rats opened their eyes and were verified with an ophthalmoscope. No such occurrence was found in the rats weaned at the age of two weeks. Preliminary studies indicate that a level of lactose as low as 5 per cent. in the synthetic liquid milk fed was the apparent cause.

[5] H. H. Love, "Application of Statistical Methods to Agricultural Research." Shanghai: The Commercial Press, Ltd. 1936.

study, using a ration in which 6 per cent. liver extract (1:20 paste) was included, rats fed butterfat made better, but insignificantly better (Fisher's "t" test)[6] gains over those fed corn oil. The average results of both these studies for the male rats are summarized in Table 2. The results on the females were quite similar in significance.

These studies indicate that, apart from differences in vitamin content, corn oil and butterfat are essentially equal in growth-promoting value for the rat.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

A TECHNIQUE FOR MOUNTING FREE-LIVING PROTOZOA

THE mounting of free-living protozoa on to microscope slides has always been a source of trouble to the protozoologist. The method of centrifuging after each stage in the processes of staining, dehydration, etc., suffers from several disadvantages. Firstly, the control of differentiation is difficult; for if over- or under-staining occurs, all the specimens in the tube are affected, and the whole must be re-treated. Secondly, since the organisms have to be centrifuged a considerable number of times in their passage through alcohols, stains, etc., it means that the cells are frequently distorted and true cytological pictures are not obtained. This is especially the case in dividing protozoa, where the protoplasm is less viscid than usual.[1]

Several methods of fixing protozoa to slides have been suggested,[2] but are unsatisfactory for one reason or another. The following method, recently developed by the writer, fixes the protozoa very securely to the slide and is simple and effective to use in practice.

The organisms are fixed in Schaudinn, and brought through 70 per cent. and 90 per cent. into absolute alcohol by gentle centrifuging. A small drop of albumen is placed on a clean slide, and a very thin film produced by smearing it with the edge of another slide —exactly as in the preparation of a blood film. A drop of the concentrated organisms is allowed to fall on to the film of albumen from a fine pipette held about an inch above the slide. The combined action of the dropping force and the rapid coagulation of the albumen by the alcohol, immediately causes the organisms to be fixed securely to the slide. These slides are then placed in absolute alcohol, and treated as ordinary sections.

This method avoids the difficulties mentioned above; the small amount of centrifuging necessary in the preliminary concentrating never being sufficient to damage the cells. The film of albumen, too, is so thin that it causes no interference with the staining reactions of the protozoa.

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[6] F. E. Croxton and D. J. Cowden, "Applied General Statistics." New York: Prentice-Hall, Inc. 1941.

[1] J. B. Gatenby and J. D. Smyth, *Quart. Jour. Micr. Sci.*, 81, 1940.

ON QUIETING PARAMECIUM WITH METHYL CELLULOSE

MARSLAND[1] has suggested an excellent method of quieting Paramecia for study by the elementary student, using Dow "Methocel," or methyl cellulose in 10 per cent. aqueous solution.

We have found in our laboratory a slight modification of Marsland's method to be even more satisfactory for our purposes. Since 10 per cent. was a little too viscous, we tried 5 per cent., and we suggest this procedure: Make a small ring of 5 per cent. Methocel, slightly smaller than the cover glass to be used. Into the center of the ring place a small drop of medium containing Paramecia. Add a cover glass. Practice teaches one how much of each to use, but less than a full drop of each is often satisfactory with small cover glasses.

This enables the student to observe normal movement for a few minutes before diffusion of the methyl cellulose has slowed him down, and then progressively increasing viscosity gradually slows him to a completely stationary position. At this point he may be placed under an oil immersion objective, and ciliary motion studied in detail. Eventually even this slows down until the cilia appear to beat with great effort.

The Dow Company was very generous in furnishing us with the methyl cellulose.

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[2] J. B. Gatenby and T. S. Painter, "Microtomist's Vade Mecum," London, 1937.

[1] Douglas A. Marsland, SCIENCE, 98: 2549, 414, November 5, 1943.

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